

TDMS No. 99024 - 07

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/F 344

**P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH
AVERAGE SEVERITY GRADES[b]**

Androstenedione

CAS Number: 63-05-8

F1_R2

Date Report Requested: 08/08/2008

Time Report Requested: 08:20:33

First Dose M/F: 02/03/03 / 02/03/03

Lab: SRI

C Number: C99024C

Lock Date: 06/29/2006

Cage Range: ALL

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Study Gender: Both

TDMSE Version: 2.0.0

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Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|----------------------------------|----------|----------|----------|----------|
| Disposition Summary | | | | |
| Animals Initially in Study | 50 | 50 | 50 | 50 |
| Early Deaths | | | | |
| Moribund Sacrifice | 22 | 9 | 17 | 13 |
| Natural Death | 7 | 8 | 4 | 10 |
| Survivors | | | | |
| Natural Death | 1 | | | |
| Terminal Sacrifice | 20 | 33 | 29 | 27 |
| Animals Examined Microscopically | 50 | 50 | 50 | 50 |
| ALIMENTARY SYSTEM | | | | |
| Esophagus | (50) | (50) | (50) | (50) |
| Foreign Body | 1 [2.0] | | | |
| Inflammation, Suppurative | 1 [3.0] | | | |
| Intestine Large, Cecum | (47) | (46) | (47) | (48) |
| Edema | | | 1 [3.0] | |
| Intestine Large, Colon | (44) | (43) | (47) | (44) |
| Edema | 2 [3.5] | 1 [3.0] | 4 [3.0] | |
| Fibrosis | 1 [2.0] | | | |
| Intestine Large, Rectum | (46) | (46) | (47) | (47) |
| Hemorrhage | | | 1 [3.0] | |
| Intestine Small, Duodenum | (48) | (47) | (49) | (47) |
| Hemorrhage | | | 1 [1.0] | |
| Intestine Small, Ileum | (44) | (46) | (47) | (44) |
| Intestine Small, Jejunum | (44) | (44) | (47) | (42) |
| Hemorrhage | | | 1 [3.0] | |
| Liver | (50) | (50) | (50) | (50) |
| Angiectasis | | 1 [2.0] | | 1 [2.0] |
| Basophilic Focus | 17 | 29 | 29 | 33 |
| Clear Cell Focus | 13 | 21 | 23 | 14 |
| Clear Cell Focus, Multiple | | | | 3 |
| Degeneration, Cystic | 10 [1.6] | 3 [2.0] | 12 [1.6] | 7 [1.6] |
| Eosinophilic Focus | 3 | 10 | 7 | 13 |
| Hematopoietic Cell Proliferation | | 1 [2.0] | | |
| Hemorrhage | | | 1 [4.0] | |
| Hepatodiaphragmatic Nodule | 7 [2.2] | 8 [2.0] | 7 [2.2] | 10 [2.0] |

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Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|---------------------------------------|----------|----------|----------|----------|
| Infiltration Cellular, Mixed Cell | 10 [1.0] | 3 [1.3] | 11 [1.1] | 4 [1.5] |
| Inflammation, Chronic | 1 [1.0] | | | |
| Mixed Cell Focus | 1 | 2 | 1 | 4 |
| Necrosis, Focal | 4 [2.0] | | 1 [2.0] | 1 [2.0] |
| Tension Lipidosis | 1 [2.0] | | | |
| Thrombosis | | | 1 [4.0] | |
| Bile Duct, Hyperplasia | 44 [1.8] | 44 [1.8] | 40 [1.7] | 43 [1.6] |
| Hepatocyte, Hyperplasia | 1 [3.0] | | 2 [2.0] | 2 [2.5] |
| Hepatocyte, Vacuolization Cytoplasmic | 25 [1.8] | 18 [1.9] | 14 [2.1] | 9 [1.4] |
| Kupffer Cell, Pigmentation | 1 [1.0] | | | |
| Mesentery | (18) | (13) | (12) | (18) |
| Accessory Spleen | 4 [2.0] | 1 [3.0] | | 3 [2.0] |
| Hemorrhage | | 1 [2.0] | | |
| Inflammation, Suppurative | 1 [2.0] | | | |
| Inflammation, Granulomatous | 1 [2.0] | | | |
| Fat, Necrosis | 13 [2.2] | 10 [2.3] | 10 [2.2] | 15 [2.2] |
| Pancreas | (50) | (50) | (50) | (50) |
| Atrophy | 17 [1.9] | 30 [2.0] | 19 [1.8] | 21 [1.7] |
| Cyst | 5 [2.4] | 3 [1.7] | 7 [2.1] | |
| Infiltration Cellular, Lymphocyte | | | | 1 [1.0] |
| Acinus, Cytoplasmic Alteration | 4 [2.5] | 3 [2.7] | 2 [3.0] | 2 [3.0] |
| Acinus, Hyperplasia, Focal | 1 [2.0] | 3 [2.3] | 3 [1.7] | 2 [2.5] |
| Arteriole, Inflammation, Chronic | | 1 [2.0] | | |
| Salivary Glands | (50) | (50) | (50) | (50) |
| Atrophy | | | | 1 [3.0] |
| Stomach, Forestomach | (50) | (50) | (50) | (50) |
| Edema | 4 [3.0] | 7 [3.1] | 4 [3.8] | 4 [3.5] |
| Erosion | 1 [2.0] | | | |
| Hemorrhage | | | 1 [2.0] | |
| Inflammation, Chronic Active | | 1 [2.0] | | |
| Ulcer | 6 [2.5] | 7 [3.0] | 4 [3.5] | 5 [2.8] |
| Epithelium, Hyperplasia | 5 [2.4] | 6 [2.3] | 3 [3.0] | 5 [2.2] |
| Stomach, Glandular | (50) | (50) | (50) | (50) |
| Edema | | | | 1 [2.0] |
| Erosion | 6 [2.0] | 2 [1.5] | 4 [1.8] | 5 [1.8] |
| Ulcer | 2 [2.5] | 1 [3.0] | 2 [2.5] | 1 [3.0] |
| Epithelium, Cyst | 1 [2.0] | | | 1 [2.0] |
| Epithelium, Hyperplasia | 1 [1.0] | | 2 [2.0] | 2 [2.0] |
| Muscularis, Hyperplasia | | | | 1 [2.0] |
| Tongue | (1) | (0) | (0) | (2) |

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Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|--|----------|----------|----------------|----------------|
| Hyperplasia, Squamous Tooth Malformation | (0) | (0) | (1) 1 [3.0] | 2 [2.0] (0) |
| CARDIOVASCULAR SYSTEM | | | | |
| Blood Vessel | (2) | (3) | (1) | (0) |
| Heart | (50) | (50) | (50) | (50) |
| Cardiomyopathy | 47 [2.0] | 47 [2.0] | 48 [2.1] | 48 [2.0] |
| Thrombosis | 6 [2.7] | 3 [3.3] | 3 [2.7] | 2 [3.0] |
| ENDOCRINE SYSTEM | | | | |
| Adrenal Cortex | (50) | (50) | (50) | (50) |
| Accessory Adrenal Cortical Nodule | 1 [1.0] | 3 [2.0] | 1 [2.0] | 1 [3.0] |
| Degeneration, Fatty | 22 [2.0] | 27 [1.9] | 25 [2.0] | 21 [1.7] |
| Hyperplasia, Focal | 5 [1.4] | 4 [1.8] | 3 [1.3] | 1 [1.0] |
| Hypertrophy, Focal | 3 [1.0] | 3 [1.0] | 2 [1.0] | 4 [1.5] |
| Hypertrophy, Diffuse | | | | 1 [2.0] |
| Necrosis | 1 [3.0] | | | |
| Bilateral, Necrosis | | 1 [3.0] | | |
| Adrenal Medulla | (50) | (50) | (50) | (50) |
| Hyperplasia | 5 [2.0] | 8 [2.0] | 6 [2.0] | 10 [1.8] |
| Infiltration Cellular, Lymphocyte | | | | 1 [2.0] |
| Islets, Pancreatic | (50) | (50) | (50) | (50) |
| Hyperplasia | 5 [1.8] | 4 [2.0] | 2 [1.5] | 9 [1.8] |
| Parathyroid Gland | (48) | (50) | (50) | (48) |
| Cyst | | 1 [3.0] | | |
| Hyperplasia | | | | 1 [3.0] |
| Pituitary Gland | (50) | (50) | (49) | (50) |
| Pars Distalis, Angiectasis | 1 [3.0] | 1 [2.0] | | 2 [3.5] |
| Pars Distalis, Cyst | 2 [1.5] | 3 [2.3] | 1 [3.0] | 4 [2.3] |
| Pars Distalis, Hyperplasia, Focal | 13 [1.7] | 15 [1.9] | 21 [1.8] | 18 [1.7] |
| Pars Intermedia, Angiectasis | | | | 1 [2.0] |
| Pars Intermedia, Cyst | | | 2 [2.0] | |
| Pars Intermedia, Hyperplasia, Focal | | | 1 [2.0] | |
| Rathke's Cleft, Cyst | | | 1 [2.0] | |
| Thyroid Gland | (50) | (50) | (50) | (50) |
| Ultimobranchial Cyst | 1 [2.0] | 1 [2.0] | 2 [1.5] | |

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| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|--------------------------------|----------|----------|----------|----------|
| C-cell, Hyperplasia | 32 [1.4] | 33 [1.2] | 26 [1.2] | 20 [1.3] |
| Follicle, Cyst | | 1 [3.0] | 5 [2.2] | 1 [2.0] |
| Follicular Cell, Hyperplasia | | 2 [1.5] | 2 [1.5] | 1 [1.0] |
| GENERAL BODY SYSTEM | | | | |
| Tissue NOS | (0) | (0) | (1) | (0) |
| GENITAL SYSTEM | | | | |
| Coagulating Gland | (0) | (3) | (2) | (0) |
| Inflammation, Suppurative | | 1 [3.0] | | |
| Epithelium, Hyperplasia | | 1 [3.0] | | |
| Epididymis | (50) | (50) | (50) | (50) |
| Atrophy | 1 [3.0] | | | |
| Degeneration | 1 [3.0] | | | |
| Inflammation, Chronic | | | | 1 [2.0] |
| Penis | (0) | (1) | (0) | (0) |
| Inflammation, Chronic | | 1 [2.0] | | |
| Preputial Gland | (50) | (50) | (50) | (50) |
| Cyst | 4 [3.0] | 2 [2.5] | | 7 [2.9] |
| Fibrosis | | | | 1 [3.0] |
| Hyperplasia | 1 [2.0] | 1 [2.0] | | 1 [2.0] |
| Inflammation, Chronic | 47 [1.7] | 48 [1.6] | 41 [1.4] | 43 [1.3] |
| Prostate | (50) | (50) | (50) | (50) |
| Inflammation, Chronic | 25 [2.0] | 24 [2.1] | 20 [2.1] | 20 [2.0] |
| Epithelium, Hyperplasia | 9 [1.9] | 18 [1.9] | 9 [2.1] | 12 [1.9] |
| Seminal Vesicle | (50) | (50) | (50) | (50) |
| Testes | (50) | (50) | (50) | (50) |
| Malformation | | | | 1 |
| Thrombosis | 1 [4.0] | | | |
| Germinal Epithelium, Atrophy | 9 [3.1] | 8 [2.8] | 10 [3.0] | 11 [2.5] |
| Interstitial Cell, Hyperplasia | 4 [1.5] | 2 [2.0] | 2 [1.0] | 2 [1.0] |
| HEMATOPOIETIC SYSTEM | | | | |
| Bone Marrow | (50) | (50) | (50) | (50) |
| Hyperplasia | 4 [2.8] | 4 [2.5] | 4 [3.5] | 7 [2.9] |

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Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|---------------------------------------|----------|----------|----------|----------|
| Myelofibrosis | 1 [4.0] | 2 [3.5] | | |
| Lymph Node | (25) | (18) | (16) | (13) |
| Mediastinal, Angiectasis | | 1 [2.0] | | |
| Mediastinal, Ectasia | 1 [3.0] | | 2 [2.5] | |
| Mediastinal, Fibrosis | 1 [3.0] | | | |
| Mediastinal, Hemorrhage | | 1 [2.0] | 1 [3.0] | |
| Mediastinal, Hyperplasia, Histiocytic | 1 [2.0] | | | |
| Mediastinal, Hyperplasia, Lymphoid | 3 [2.3] | 3 [3.0] | | |
| Pancreatic, Angiectasis | | | | 1 [2.0] |
| Pancreatic, Atrophy | 1 [4.0] | | | |
| Pancreatic, Ectasia | 3 [3.0] | 1 [3.0] | 2 [2.5] | |
| Pancreatic, Hemorrhage | 1 [3.0] | | 1 [4.0] | |
| Pancreatic, Hyperplasia, Histiocytic | 7 [2.3] | | 3 [2.3] | 2 [1.5] |
| Pancreatic, Hyperplasia, Lymphoid | 1 [3.0] | | | |
| Pancreatic, Necrosis | | 1 [3.0] | | |
| Lymph Node, Mandibular | (1) | (0) | (1) | (2) |
| Lymph Node, Mesenteric | (50) | (50) | (50) | (50) |
| Atrophy | 1 [3.0] | | | |
| Ectasia | 3 [2.7] | 5 [2.4] | 7 [2.3] | 5 [2.2] |
| Fibrosis | 1 [3.0] | | | |
| Hemorrhage | | | 2 [3.0] | |
| Hyperplasia, Histiocytic | 25 [1.4] | 13 [1.2] | 25 [1.5] | 19 [1.5] |
| Hyperplasia, Lymphoid | 1 [2.0] | 2 [2.0] | 1 [2.0] | 1 [3.0] |
| Infiltration Cellular, Eosinophil | 1 [2.0] | | | |
| Infiltration Cellular, Plasma Cell | 1 [3.0] | | | |
| Pigmentation | | | | 2 [1.0] |
| Spleen | (50) | (50) | (50) | (50) |
| Accessory Spleen | | 1 [2.0] | 1 [2.0] | |
| Fibrosis | 6 [2.8] | 1 [2.0] | 4 [2.8] | |
| Hematopoietic Cell Proliferation | 2 [2.0] | | 4 [2.5] | 2 [2.0] |
| Hemorrhage | 2 [3.0] | | | |
| Hyperplasia, Histiocytic | 1 [2.0] | | | 1 [3.0] |
| Hyperplasia, Lymphoid | 1 [3.0] | | | |
| Necrosis | 2 [3.5] | 1 [4.0] | 1 [3.0] | |
| Pigmentation | 12 [2.1] | 12 [2.1] | 8 [2.1] | 12 [2.3] |
| Lymphoid Follicle, Hyperplasia | | 3 [2.0] | 4 [2.8] | 3 [2.7] |
| Red Pulp, Hyperplasia | | | 1 [3.0] | |
| Thymus | (50) | (50) | (50) | (49) |
| Atrophy | | | 2 [3.0] | |
| Cyst | | | 1 [3.0] | |

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Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|-----------------------------|----------|----------|----------|----------|
| Hemorrhage | | 1 [2.0] | 1 [2.0] | |
| Hyperplasia, Lymphoid | 2 [2.5] | | | |
| INTEGUMENTARY SYSTEM | | | | |
| Mammary Gland | (48) | (50) | (50) | (50) |
| Cyst | 8 [2.5] | 4 [2.3] | 4 [2.8] | 11 [2.2] |
| Hyperplasia | 38 [1.7] | 37 [1.6] | 33 [1.7] | 42 [1.5] |
| Inflammation, Granulomatous | 1 [2.0] | | | |
| Skin | (50) | (50) | (50) | (50) |
| Cyst Epithelial Inclusion | 3 | 1 | 1 | 2 [3.0] |
| Fibrosis | | 2 [3.0] | 1 [3.0] | 3 [1.7] |
| Hyperkeratosis | 5 [2.6] | 3 [3.0] | 6 [2.5] | 7 [2.6] |
| Inflammation, Suppurative | | | | 1 [2.0] |
| Inflammation, Granulomatous | | | | 1 [3.0] |
| Inflammation, Chronic | | | 1 [3.0] | 1 [3.0] |
| Ulcer | | | | 1 [3.0] |
| Epidermis, Hyperplasia | 3 [2.3] | 1 [2.0] | 3 [2.0] | 3 [2.0] |
| MUSCULOSKELETAL SYSTEM | | | | |
| Bone | (50) | (50) | (50) | (50) |
| Cranium, Osteopetrosis | 1 [3.0] | | | 1 [2.0] |
| Skeletal Muscle | (8) | (1) | (3) | (5) |
| Fibrosis | 3 [2.0] | | 2 [2.0] | 1 [2.0] |
| NERVOUS SYSTEM | | | | |
| Brain | (50) | (50) | (50) | (50) |
| Compression | 13 [2.4] | 8 [2.6] | 7 [2.7] | 9 [2.4] |
| Gliosis | 1 [2.0] | | | |
| Hemorrhage | 3 [2.7] | | 2 [2.5] | 4 [2.5] |
| Necrosis | | | | 2 [3.0] |
| Spinal Cord | (6) | (1) | (0) | (5) |
| RESPIRATORY SYSTEM | | | | |
| Lung | (50) | (50) | (50) | (50) |

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|--|----------|----------|----------|----------|
| Congestion | | | 1 [3.0] | |
| Foreign Body | | | 1 [2.0] | |
| Hemorrhage | 1 [2.0] | 1 [2.0] | 1 [1.0] | 1 [2.0] |
| Infiltration Cellular, Histiocyte | 17 [1.6] | 17 [1.2] | 18 [1.2] | 18 [1.1] |
| Inflammation, Granulomatous | | 1 [2.0] | 1 [2.0] | 1 [2.0] |
| Inflammation, Chronic | | | 1 [1.0] | 3 [1.7] |
| Metaplasia, Osseous | | 1 [1.0] | 1 [2.0] | |
| Alveolar Epithelium, Hyperplasia | 6 [2.3] | 7 [2.1] | 8 [2.0] | 4 [2.0] |
| Serosa, Cyst | | | | 1 [2.0] |
| Nose | (50) | (50) | (50) | (50) |
| Foreign Body | 5 [1.8] | 13 [1.7] | 5 [1.8] | |
| Infiltration Cellular, Lymphocyte | | | 1 [2.0] | |
| Inflammation, Suppurative | 3 [2.0] | 4 [2.5] | 1 [2.0] | 1 [2.0] |
| Inflammation, Chronic | 4 [2.3] | 3 [2.0] | 5 [1.4] | 1 [2.0] |
| Nasolacrimal Duct, Inflammation, Chronic | | | | 1 [2.0] |
| Respiratory Epithelium, Hyperplasia | 8 [2.4] | 11 [2.2] | 7 [2.1] | 3 [2.0] |
| Sinus, Inflammation, Suppurative | 1 [2.0] | | | |
| Vomeranasal Organ, Atrophy | | | 1 [2.0] | |
| SPECIAL SENSES SYSTEM | | | | |
| Eye | (48) | (46) | (50) | (49) |
| Cataract | 1 [4.0] | | 1 [3.0] | 2 [2.5] |
| Ciliary Body, Hyperplasia | 1 [2.0] | | | |
| Retina, Degeneration | 1 [2.0] | 1 [2.0] | 1 [4.0] | 4 [2.0] |
| Retina, Edema | | | | 1 [2.0] |
| Sclera, Metaplasia, Osseous | | 3 [1.3] | 2 [2.0] | 1 [1.0] |
| Harderian Gland | (50) | (50) | (50) | (50) |
| Infiltration Cellular, Lymphocyte | | | 1 [2.0] | |
| Inflammation, Chronic | | | | 1 [2.0] |
| Necrosis | 1 [2.0] | | | |
| Zymbal's Gland | (0) | (0) | (1) | (0) |
| URINARY SYSTEM | | | | |
| Kidney | (49) | (50) | (50) | (50) |
| Cyst | | | | 1 [1.0] |
| Hydronephrosis | | | | 1 [3.0] |
| Infarct | 3 [2.3] | 1 [2.0] | | |

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Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS MALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|--|----------|----------|----------|----------|
| Nephropathy | 42 [1.6] | 48 [2.0] | 46 [1.9] | 44 [2.0] |
| Renal Tubule, Accumulation, Hyaline Droplet | 1 [3.0] | 1 [3.0] | | 1 [4.0] |
| Renal Tubule, Necrosis | 1 [3.0] | 1 [3.0] | 2 [2.5] | |
| Renal Tubule, Pigmentation | 5 [2.4] | 2 [2.0] | 6 [2.3] | 6 [1.7] |
| Urinary Bladder | (50) | (50) | (50) | (50) |
| Calculus Micro Observation Only | | 1 [2.0] | | |
| Hemorrhage | | | | 1 [3.0] |
| Inflammation, Chronic | | 1 [3.0] | | |
| Transitional Epithelium, Hyperplasia | | 2 [2.5] | | |

*** END OF MALE ***

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|---------------------------------------|----------|----------|----------|----------|
| Disposition Summary | | | | |
| Animals Initially in Study | 50 | 50 | 50 | 50 |
| Early Deaths | | | | |
| Moribund Sacrifice | 10 | 7 | 12 | 9 |
| Natural Death | 2 | 6 | 5 | 4 |
| Survivors | | | | |
| Natural Death | | 1 | | |
| Terminal Sacrifice | 38 | 36 | 33 | 37 |
| Animals Examined Microscopically | 50 | 50 | 50 | 50 |
| ALIMENTARY SYSTEM | | | | |
| Intestine Large, Rectum | (49) | (47) | (47) | (48) |
| Edema | 1 [2.0] | | | |
| Intestine Small, Ileum | (48) | (46) | (45) | (48) |
| Serosa, Inflammation, Chronic | 1 [2.0] | | | |
| Liver | (50) | (50) | (50) | (50) |
| Angiectasis | | 1 [2.0] | | 1 [2.0] |
| Basophilic Focus | 47 | 46 | 42 | 38 |
| Clear Cell Focus | 14 | 10 | 11 | 14 |
| Degeneration, Cystic | | | | 1 [2.0] |
| Eosinophilic Focus | 5 | | 4 | |
| Fibrosis | 1 [2.0] | 1 [1.0] | | |
| Hematopoietic Cell Proliferation | 1 [1.0] | | | |
| Hemorrhage | | | | 1 [1.0] |
| Hepatodiaphragmatic Nodule | 10 [2.1] | 9 [1.7] | 11 [2.1] | 9 [2.3] |
| Infiltration Cellular, Mixed Cell | 21 [1.0] | 33 [1.2] | 32 [1.2] | 31 [1.2] |
| Mixed Cell Focus | 1 | | 2 | |
| Necrosis, Focal | | | 1 [1.0] | 1 [2.0] |
| Bile Duct, Hyperplasia | 12 [1.3] | 16 [1.3] | 18 [1.3] | 24 [1.2] |
| Centrilobular, Necrosis | | | | 1 [1.0] |
| Hepatocyte, Vacuolization Cytoplasmic | 6 [1.8] | 4 [3.0] | 7 [2.6] | 5 [2.4] |
| Kupffer Cell, Pigmentation | 2 [1.5] | | | |
| Mesentery | (13) | (14) | (15) | (15) |
| Accessory Spleen | 2 | | 3 [1.7] | 2 [2.0] |
| Fat, Necrosis | 12 [2.3] | 14 [2.2] | 14 [2.1] | 12 [2.0] |
| Oral Mucosa | (0) | (1) | (0) | (0) |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|-----------------------------------|----------|----------|----------|----------|
| Pancreas | (50) | (50) | (50) | (50) |
| Atrophy | 10 [1.6] | 10 [1.8] | 16 [1.8] | 26 [1.6] |
| Cyst | 3 [2.3] | 7 [1.7] | 4 [1.5] | 2 [1.5] |
| Infiltration Cellular, Lymphocyte | | 1 [2.0] | 3 [2.0] | 3 [2.0] |
| Acinus, Cytoplasmic Alteration | | 4 [2.8] | 1 [3.0] | 2 [3.0] |
| Acinus, Hyperplasia, Focal | | | 1 [2.0] | 3 [2.0] |
| Salivary Glands | (50) | (50) | (50) | (50) |
| Atrophy | | 1 [2.0] | | |
| Vacuolization Cytoplasmic | | 1 [4.0] | | |
| Stomach, Forestomach | (50) | (50) | (50) | (50) |
| Edema | 1 [4.0] | 3 [2.3] | 2 [3.5] | 3 [2.7] |
| Inflammation, Chronic Active | 1 [3.0] | | | |
| Ulcer | 2 [3.5] | 2 [3.0] | 2 [2.5] | 2 [3.0] |
| Epithelium, Hyperplasia | 3 [3.0] | 1 [2.0] | 2 [2.5] | 6 [2.5] |
| Stomach, Glandular | (50) | (50) | (50) | (50) |
| Edema | | | | 2 [2.5] |
| Erosion | | | | 3 [1.7] |
| Ulcer | | | 2 [1.5] | 1 [2.0] |
| Epithelium, Hyperplasia | 1 [2.0] | 2 [2.5] | | 1 [2.0] |
| Tongue | (1) | (0) | (1) | (1) |
| Hyperkeratosis | | | | 1 [2.0] |
| Epithelium, Hyperplasia | 1 [2.0] | | | |
| CARDIOVASCULAR SYSTEM | | | | |
| Heart | (50) | (50) | (50) | (50) |
| Cardiomyopathy | 46 [1.7] | 43 [1.7] | 43 [1.7] | 48 [1.9] |
| Thrombosis | | 2 [2.5] | 1 [2.0] | 1 [3.0] |
| ENDOCRINE SYSTEM | | | | |
| Adrenal Cortex | (50) | (50) | (50) | (50) |
| Accessory Adrenal Cortical Nodule | 1 [2.0] | 3 [2.0] | 1 [2.0] | |
| Angiectasis | 1 [2.0] | | | |
| Degeneration, Fatty | 15 [1.9] | 20 [1.9] | 24 [1.8] | 13 [1.9] |
| Hematopoietic Cell Proliferation | | 2 [1.5] | | 1 [1.0] |
| Hyperplasia, Focal | 1 [2.0] | 4 [1.5] | 1 [2.0] | 2 [2.0] |
| Hypertrophy, Focal | 12 [1.8] | 10 [2.1] | 9 [1.8] | 2 [1.0] |
| Hypertrophy, Diffuse | | 1 [2.0] | | |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|-------------------------------------|----------|----------|----------|----------|
| Necrosis | | 1 [2.0] | | |
| Capsule, Developmental Malformation | | 1 | | |
| Adrenal Medulla | (50) | (50) | (50) | (50) |
| Hyperplasia | 1 [2.0] | 1 [2.0] | 3 [2.3] | 2 [2.0] |
| Islets, Pancreatic | (50) | (50) | (50) | (50) |
| Hyperplasia | | 4 [1.8] | 1 [2.0] | 11 [1.8] |
| Parathyroid Gland | (49) | (48) | (48) | (45) |
| Hyperplasia | | | | 1 [2.0] |
| Pituitary Gland | (50) | (50) | (49) | (50) |
| Pars Distalis, Angiectasis | | 1 [3.0] | 1 [3.0] | 3 [2.3] |
| Pars Distalis, Cyst | 18 [2.3] | 12 [2.4] | 14 [2.4] | 13 [2.5] |
| Pars Distalis, Hyperplasia, Focal | 20 [2.0] | 20 [1.9] | 14 [1.8] | 19 [1.7] |
| Pars Intermedia, Angiectasis | 1 [1.0] | | | |
| Rathke's Cleft, Cyst | 3 [3.0] | 1 [1.0] | 4 [2.5] | |
| Thyroid Gland | (50) | (50) | (50) | (50) |
| Ultimobranchial Cyst | | | 2 [1.5] | 1 [1.0] |
| C-cell, Hyperplasia | 27 [1.8] | 33 [1.7] | 24 [1.5] | 25 [1.7] |
| Follicle, Cyst | | 1 [2.0] | 2 [2.0] | 1 [2.0] |
| Follicular Cell, Hyperplasia | 1 [1.0] | | | |

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

| | | | | |
|-----------------------------------|----------|----------|----------|----------|
| Clitoral Gland | (50) | (50) | (50) | (50) |
| Cyst | 6 [2.8] | 8 [2.8] | 8 [3.1] | 4 [2.8] |
| Hyperplasia | 3 [2.7] | 4 [3.0] | | 3 [2.3] |
| Inflammation, Suppurative | 1 [2.0] | | 1 [3.0] | 1 [2.0] |
| Inflammation, Chronic | 23 [1.0] | 26 [1.2] | 18 [1.4] | 24 [1.3] |
| Ovary | (50) | (50) | (50) | (50) |
| Angiectasis | | | | 1 [2.0] |
| Cyst | 3 [2.7] | 5 [2.8] | 2 [3.0] | 1 [3.0] |
| Infiltration Cellular, Histiocyte | | | | 1 [2.0] |
| Bursa, Dilatation | 6 [2.8] | 6 [3.0] | 2 [3.0] | 6 [3.0] |
| Corpus Luteum, Hyperplasia | | 1 [3.0] | | |
| Follicle, Cyst | | | | 1 [2.0] |
| Interstitial Cell, Cyst | | | | 1 [2.0] |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|---|----------|----------|----------|----------|
| Uterus | (50) | (50) | (50) | (50) |
| Decidual Reaction | | | 1 [3.0] | |
| Hemorrhage | | 1 [2.0] | 1 [4.0] | 1 [3.0] |
| Hyperplasia, Cystic | 9 [1.8] | 8 [1.9] | 11 [1.6] | 14 [1.9] |
| Inflammation, Suppurative | 1 [3.0] | | | |
| Thrombosis | | 1 [4.0] | | |
| Epithelium, Hyperplasia | | | 2 [2.0] | |
| HEMATOPOIETIC SYSTEM | | | | |
| Bone Marrow | (50) | (50) | (50) | (50) |
| Atrophy | | 1 [2.0] | 1 [2.0] | |
| Hyperplasia | 3 [3.7] | 6 [2.0] | 5 [2.8] | 1 [3.0] |
| Thrombosis | | 1 [2.0] | | |
| Lymph Node | (5) | (10) | (16) | (10) |
| Congestion | | | 1 [2.0] | |
| Deep Cervical, Ectasia | | | 1 [2.0] | |
| Deep Cervical, Necrosis | 1 [4.0] | | | |
| Mediastinal, Ectasia | | 2 [3.0] | 1 [2.0] | |
| Mediastinal, Hemorrhage | | 3 [2.0] | 1 [3.0] | 1 [2.0] |
| Mediastinal, Hyperplasia, Lymphoid | 2 [2.0] | 2 [2.5] | 3 [2.0] | |
| Mediastinal, Infiltration Cellular, Mast Cell | 1 [2.0] | | | |
| Mediastinal, Pigmentation | 1 [2.0] | | | |
| Pancreatic, Ectasia | | | 1 [3.0] | |
| Pancreatic, Hemorrhage | 1 [3.0] | 2 [2.0] | 3 [2.3] | 2 [2.0] |
| Pancreatic, Hyperplasia, Histiocytic | | | 1 [2.0] | |
| Pancreatic, Pigmentation | | | | 1 [3.0] |
| Lymph Node, Mandibular | (0) | (0) | (0) | (1) |
| Lymph Node, Mesenteric | (50) | (50) | (49) | (50) |
| Ectasia | 2 [2.0] | | 3 [2.3] | 4 [2.3] |
| Hemorrhage | | | 1 [2.0] | |
| Hyperplasia, Histiocytic | 29 [1.7] | 34 [1.8] | 24 [1.8] | 19 [1.6] |
| Hyperplasia, Lymphoid | | 1 [3.0] | 1 [2.0] | 1 [2.0] |
| Pigmentation | 1 [2.0] | | 2 [2.0] | |
| Spleen | (50) | (49) | (50) | (50) |
| Fibrosis | | | 1 [3.0] | |
| Hematopoietic Cell Proliferation | 5 [2.0] | 3 [2.7] | 6 [1.5] | 2 [1.5] |
| Hemorrhage | | 1 [3.0] | 1 [3.0] | 1 [4.0] |
| Hyperplasia, Lymphoid | | | | 1 [2.0] |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|-----------------------------------|----------|----------|----------|----------|
| Infiltration Cellular, Mixed Cell | | | | 1 [1.0] |
| Pigmentation | 43 [2.0] | 44 [2.0] | 39 [1.8] | 36 [1.7] |
| Lymphoid Follicle, Hyperplasia | 1 [3.0] | 2 [3.5] | 3 [2.7] | 11 [2.7] |
| Thymus | (50) | (50) | (49) | (50) |
| Atrophy | | | | 1 [2.0] |
| Hemorrhage | | 1 [2.0] | | |
| INTEGUMENTARY SYSTEM | | | | |
| Mammary Gland | (50) | (50) | (50) | (50) |
| Cyst | 15 [2.1] | 3 [1.7] | 9 [2.1] | 3 [2.7] |
| Hyperplasia | 48 [2.2] | 40 [2.3] | 35 [2.0] | 23 [1.8] |
| Inflammation, Suppurative | | | | 1 [4.0] |
| Skin | (50) | (50) | (50) | (50) |
| Cyst Epithelial Inclusion | | 1 [2.0] | | 1 [3.0] |
| Hyperkeratosis | | 1 [3.0] | | 2 [3.0] |
| MUSCULOSKELETAL SYSTEM | | | | |
| Bone | (50) | (50) | (50) | (50) |
| Hyperostosis | | | | 1 [3.0] |
| Skeletal Muscle | (0) | (1) | (0) | (0) |
| Inflammation, Chronic | | 1 [2.0] | | |
| NERVOUS SYSTEM | | | | |
| Brain | (50) | (50) | (50) | (50) |
| Compression | 6 [2.2] | 10 [2.3] | 4 [2.5] | 5 [2.4] |
| Hemorrhage | 1 [3.0] | | | 1 [2.0] |
| Hydrocephalus | 1 [2.0] | 1 [3.0] | | |
| RESPIRATORY SYSTEM | | | | |
| Lung | (50) | (50) | (50) | (50) |
| Congestion | | 1 [3.0] | | |
| Emphysema | | 1 [3.0] | | |
| Hemorrhage | | 1 [1.0] | | |
| Infiltration Cellular, Histiocyte | 31 [1.0] | 37 [1.2] | 26 [1.1] | 27 [1.1] |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|---|----------|----------|----------|----------|
| Inflammation, Chronic | 1 [2.0] | 1 [2.0] | 1 [2.0] | 1 [2.0] |
| Pigmentation | | 1 [2.0] | | |
| Alveolar Epithelium, Hyperplasia | 12 [1.9] | 13 [1.5] | 11 [1.9] | 10 [1.6] |
| Artery, Hypertrophy | | 1 [2.0] | | |
| Nose | (50) | (50) | (50) | (50) |
| Foreign Body | 6 [1.7] | 4 [1.8] | 6 [1.5] | 3 [1.3] |
| Inflammation, Suppurative | 3 [2.0] | 2 [2.0] | 3 [2.3] | |
| Inflammation, Chronic | 3 [2.0] | 2 [3.0] | 1 [3.0] | |
| Respiratory Epithelium, Hyperplasia | 7 [2.0] | 8 [2.0] | 1 [2.0] | 1 [2.0] |
| SPECIAL SENSES SYSTEM | | | | |
| Ear | (0) | (1) | (0) | (0) |
| Inflammation, Suppurative | | 1 [3.0] | | |
| Eye | (49) | (48) | (47) | (49) |
| Atrophy | 1 [4.0] | 1 [3.0] | | 1 [3.0] |
| Cataract | 3 [3.7] | | | 1 [3.0] |
| Cornea, Inflammation, Chronic | | 1 [1.0] | | |
| Retina, Degeneration | | 1 [3.0] | 3 [3.0] | |
| Sclera, Metaplasia, Osseous | 1 [2.0] | | 1 [2.0] | |
| Harderian Gland | (50) | (50) | (50) | (50) |
| Infiltration Cellular, Lymphocyte | | | 1 [1.0] | |
| Zymbal's Gland | (0) | (0) | (1) | (0) |
| URINARY SYSTEM | | | | |
| Kidney | (50) | (49) | (50) | (50) |
| Cyst | 2 [3.0] | | | 1 [3.0] |
| Glomerulosclerosis | | 1 [3.0] | 1 [4.0] | |
| Infarct | 2 [2.5] | | 1 [2.0] | |
| Nephropathy | 48 [1.1] | 44 [1.1] | 43 [1.0] | 43 [1.1] |
| Renal Tubule, Accumulation, Hyaline | 3 [2.7] | | | 2 [2.5] |
| Droplet | | | | |
| Renal Tubule, Necrosis | | | | 1 [2.0] |
| Renal Tubule, Pigmentation | 1 [3.0] | | 2 [2.5] | 3 [3.3] |
| Renal Tubule, Vacuolization Cytoplasmic | | 1 [3.0] | | |
| Urinary Bladder | (50) | (50) | (50) | (50) |

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

TDMS No. 99024 - 07

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH
AVERAGE SEVERITY GRADES[b]

Date Report Requested: 08/08/2008

Test Type: CHRONIC

Androstenedione

Time Report Requested: 08:20:33

Route: GAVAGE

CAS Number: 63-05-8

First Dose M/F: 02/03/03 / 02/03/03

Species/Strain: RATS/F 344

Lab: SRI

| FISCHER 344 RATS FEMALE | 0 MG/KG | 10 MG/KG | 20 MG/KG | 50 MG/KG |
|-------------------------|---------|----------|----------|----------|
|-------------------------|---------|----------|----------|----------|

*** END OF REPORT ***

a - Number of animals examined microscopically at site and number of animals with lesion
b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)